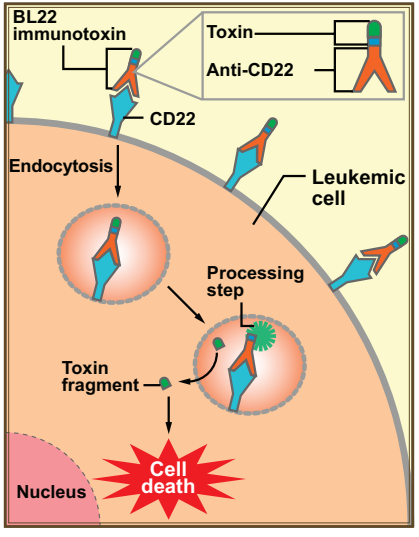
Fast Track to the Clinic

In 2008, Ira Pastan, M.D., Co-Chief of CCR's Laboratory of Molecular Biology (LMB), told *CCR connections*, "Since I was a physician trained to do research, I wanted to use what I knew to do something relevant to the treatment of cancer." [See "A Better Immunotoxin," *CCR connections* Vol. 2, No. 1]. That ambition received a major boost earlier this year when a drug developed in his laboratory—moxetumomab pasudotox—leap-frogged from a phase 1 dose-escalation trial directly into a fully fledged phase 3 multicenter trial to confirm efficacy.

Phase 1 trials are preliminary by design, and yet 49 patients with chemotherapy-resistant hairy cell leukemia (HCL) saw their tumors shrink with the drug treatment and half of those saw their tumors completely disappear. Based on the dramatic positive outcomes observed, the U.S. Food and Drug Administration agreed that the more foundational steps of phase 2 trials could be bypassed. The first patients have already been enrolled in the phase 3 trial, which is being led by Robert J. Kreitman, M.D., Head of the LMB's Clinical Immunotherapy Section, and others.

Moxetumomab pasudotox is an immunotoxin comprising one part targeting antibody and one part lethal toxin. The targeting antibody seeks out differentiated B cells, which then internalize the toxin. Pastan with his colleague David Fitzgerald, Ph.D., pioneered this technology by engineering derivatives of a naturally occurring bacterial toxin. AstraZeneca subsidiary MedImmune licensed the technology from NCI and has worked with NCI's Cancer Therapy Evaluation Program (CTEP) to further its clinical development.



(Image: I. Pastan, CCR)

Moxetumomab pasudotox binds CD22 receptors on the surface of cancerous B cells, where it is internalized and processed to release its toxic payload.